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### Deposited in DRO:

18 September 2017

### Version of attached file:

Accepted Version

### Peer-review status of attached file:

Peer-reviewed

### Citation for published item:

Hryniv, Ostap and Martínez Esteban, Antonio (2017) 'Stochastic model of microtubule dynamics.', *Journal of statistical physics.*, 169 (1). pp. 203-222.

### Further information on publisher's website:

<https://doi.org/10.1007/s10955-017-1855-2>

### Publisher's copyright statement:

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### Additional information:

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# Stochastic model of microtubule dynamics

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August 2, 2017

## Abstract

We introduce a continuous time stochastic process on strings made of two types of particle, whose dynamics mimics that of microtubules in a living cell. The long term behaviour of the system is described in terms of the velocity  $v$  of the string end. We show that  $v$  is an analytic function of its parameters and study its monotonicity properties. We give a complete characterisation of the phase diagram of the model and derive several criteria of the growth ( $v > 0$ ) and the shrinking ( $v < 0$ ) regimes of the dynamics.

**Keywords** microtubules phase transition birth-and-death process renewal decomposition stochastic domination coupling

**Mathematics Subject Classification (2010)** 60K35 82C22 82C41

## 1 Introduction

Microtubules are key structural components of the cytoskeleton, which play a vital role in a number of cellular processes. The dynamics of these tubular polymers alternates between periods of rapid growth and periods of even more rapid shrinking; the transition from growth to shrinking is called ‘catastrophe’ while that from shrinking to growth is called ‘rescue’ [4, 8]. This phenomenon of dynamical instability makes microtubules responsible for supporting the shape of

the cell, facilitating intracellular transport and enabling chromosome separation during mitosis.

Microtubules grow by polymerisation of  $\alpha$ - $\beta$  dimers of tubulin. The polarity of the latter induces polarity of the microtubule, whose plus end (terminating with the  $\beta$ -subunit) exhibits the dynamical instability behaviour. The minus end of microtubule terminates with the  $\alpha$ -subunit; in animal cells it is often attached to centrosomes [4]. When the minus end of a microtubule is free, its dynamics is known to be much slower than that of the plus end [11]. A study of the interplay between catastrophes and rescues is thus naturally reduced to the dynamics of the plus end of microtubule.

During polymerisation the tubulin complexes bind guanosine triphosphate (GTP) molecules [12], which after the assembly spontaneously hydrolyse to guanosine diphosphate (GDP) molecules. It is known [13] that the GDP-tubulin complexes at the plus end of the microtubule are more prone to depolymerisation compared to the GTP-tubulin complexes, which makes the GTP to GDP hydrolysis an essential ingredient of the dynamic instability, in addition to polymerisation and depolymerisation of individual tubulin complexes.

An important characteristics of the microtubule behaviour is the velocity of its active plus end. Given that *in vivo* the concentration of tubulin is not necessarily constant, it is crucial to understand how this velocity depends on the rates of the main moves of the dynamics. Here we study the nature of such dependence in the case of a one-dimensional model inspired by [1]; an interesting feature of the original model is that it exhibits the so-called re-entrant phase transition in a subregion of the parameter space [6].

A single protofilament model of microtubules [1] treats the latter as strings composed of two types of particle— $\oplus$  and  $\ominus$  monomers—whose dynamics is subject to attachment, detachment and conversion (hydrolysis); here the  $\oplus$  monomers and the  $\ominus$  monomers correspond to the GTP-tubulin and the GDP-tubulin complexes respectively. Long term properties of the model were rigorously studied in [5, 7]. In particular, it has been shown that the dynamics of the active end of the microtubule can be described in terms of velocity, which is an analytic function of the rates; in addition, under a suitable ordering of the attachment rates, the velocity is a decreasing function of the detachment rate and an increasing function of the attachment rates. However, this ‘regular’ behaviour is not universal: in a region in the complementary part of the parameter space the velocity is subject to the re-entrant phase transition [6], where a larger detachment rate leads to a faster growth.

The purpose of this note is to extend the results in [5, 7] to the case of a general single protofilament model of microtubules, which is a one-dimensional analogue of the full model from [10]. This general model allows depolymerisation of the GTP-tubulin complexes, a phenomenon known to exist [4], though at a very low rate. We show that as long as the attachment rates are ordered as in [5], the general model exhibits the ‘regular’ behaviour described above, irrespective of the values of the detachment rates.

## 1.1 The model

As time progresses, spontaneous hydrolysis attempts to transform all internal GTP-tubulin units into GDP-tubulin units. This stochastic mechanism is responsible for keeping the total number of GTP-complexes ‘essentially bounded’ and mostly located near the active plus end of the microtubule. In this regime the microtubule typically consists of relatively long sequence of GDP-tubulin complexes with a small number of GTP-complexes, which have polymerised relatively recently compared to the tubulin subunits deep inside the microtubule and thus had not enough time to hydrolyse. Occasionally the microtubule can lose its last GTP-complex and enter the fast shrinking phase, a ‘catastrophe’. Below we combine this observation together with statistically homogeneous, at intermediate time scales, nature of microtubule dynamics to both introduce the velocity of the active end of microtubule and study its dependence on parameters of the model. This velocity is shown to control the large term behaviour of microtubule.

Informally, we think of microtubules as long strings  $\cdots \odot \odot \odot$ , where each monomer  $\odot$  is either in  $\oplus$  state (GTP) or in  $\ominus$  state (GDP). Given four positive parameters  $\lambda^+$ ,  $\lambda^-$ ,  $\mu^+$  and  $\mu^-$ , the dynamics of these strings consists of attachment moves (at rate  $\lambda^+$  or  $\lambda^-$ ), detachment moves (at rate  $\mu^+$  or  $\mu^-$ ) and independent hydrolysis of individual  $\oplus$  monomers into  $\ominus$  monomers at rate 1. Schematically, the transitions are as follows:

$$\begin{array}{llll}
\cdots \odot \odot \odot \oplus & \mapsto & \cdots \odot \odot \odot \oplus \oplus & \text{rate } \lambda^+, \\
\cdots \odot \odot \odot \ominus & \mapsto & \cdots \odot \odot \odot \ominus \oplus & \text{rate } \lambda^-, \\
\cdots \odot \odot \odot \odot \oplus & \mapsto & \cdots \odot \odot \odot \odot & \text{rate } \mu^+, \\
\cdots \odot \odot \odot \odot \ominus & \mapsto & \cdots \odot \odot \odot \odot & \text{rate } \mu^-, \\
\cdots \odot \odot \oplus \dots & \mapsto & \cdots \odot \odot \ominus \dots & \text{rate } 1,
\end{array}$$

where  $\odot$  denotes either  $\oplus$  or  $\ominus$  (if irrelevant for the move in question) and the last, hydrolysis, move applies to each  $\oplus$  monomer (including the one at the active end of the microtubule, if in state  $\oplus$ ) independently of any other move. The (combined) rate of (any) hydrolysis move at any time is thus proportional to the current total number of  $\oplus$  monomers belonging to the microtubule. Notice that the rate of the attachment move depends on the state of the end monomer of the microtubule. The velocity of the active end can be formally defined as the relative change of length of the microtubule (equivalently, the position of its active end) per unit of time, see (1.6) below.

This model is non-reversible (the hydrolysis transformation cannot be inverted) and evolves through a sequence of transitions between ‘typical’ states with relatively large number of  $\oplus$  monomers (determined by the values of the rates  $\lambda^\pm$  and  $\mu^\pm$ ) during the ‘rescue’ phase and the states without  $\oplus$  monomers during the shrinking phase (‘catastrophe’). The statistical homogeneity of the dynamics together with good control over the duration of metastable transitions leading to the loss of the last  $\oplus$  monomer (at the start of each shrinking phase) allow to describe the long term behaviour of the model by observing the latter

at the starting points of the ‘catastrophes’.

Formally, the model studied here is as follows. Following [7], we represent microtubules as semi-infinite strings of monomers,

$$\mathbf{s} = \dots s_2 s_1 s_0 ,$$

where  $s_k \in \{\oplus, \ominus\}$  for all  $k \geq 0$ . Monomer  $s_0$  is referred to as the **active end** of  $\mathbf{s}$ . Assuming that the initial state of a microtubule contains only a finite number of  $\oplus$  monomers, the dynamics introduced below almost surely preserves this property at all subsequent times. In other words, during time intervals when  $\mathbf{s}$  contains  $\oplus$  monomers, there is  $k \geq 0$  such that  $s_k = \oplus$  and  $s_n = \ominus$  for all  $n > k$ ; *i.e.*, monomer  $s_k$  is the left-most  $\oplus$  monomer in  $\mathbf{s}$ . The finite string  $\mathbf{w} = s_k \dots s_1 s_0$  contains all  $\oplus$  monomers currently present in  $\mathbf{s}$ , and is called the **populated zone** or the **head** of  $\mathbf{s}$  [1]. Obviously, the state of a microtubule is uniquely described by its head  $\mathbf{w}$  and the position of its active end  $s_0$ .

To formally define the dynamics of microtubules, we introduce further notation. Given a two-symbol alphabet  $\{\oplus, \ominus\}$ , let

$$\mathcal{S} = \bigcup_{k \geq 0} \{\oplus, \ominus\}^k$$

be the collection of all finite strings, including the empty one. Then a **head** is a word in

$$\mathcal{W} = \{\emptyset\} \cup \bigcup_{k \geq 0} \left\{ \mathbf{w} = w_k \dots w_1 w_0 \in \{\oplus, \ominus\}^{k+1} \text{ with } w_k = \oplus \right\} \subset \mathcal{S}.$$

It is convenient to disjointly decompose

$$\mathcal{W} = \mathcal{W}_+ \cup \mathcal{W}_- , \tag{1.1}$$

where  $\mathcal{W}_+$  is the set of all plus-heads  $\mathbf{w}$  (*i.e.*, ending with a  $\oplus$  symbol,  $\mathbf{w} = \mathbf{w}'\oplus$ ), and  $\mathcal{W}_-$  contains all remaining heads (*i.e.*, the empty head  $\emptyset$  and all non-empty heads  $\mathbf{w}$  ending with  $\ominus$ ,  $\mathbf{w} = \mathbf{w}''\ominus$ ).

For any finite string  $\mathbf{s} \in \mathcal{S}$ , write  $|\mathbf{s}|$  for the length of  $\mathbf{s}$  (the total number of symbols in  $\mathbf{s}$ ), and denote by  $\|\mathbf{s}\|$  the number of  $\oplus$  symbols in  $\mathbf{s}$ . Given two strings  $\mathbf{s}' = s'_{k-1} \dots s'_0$  and  $\mathbf{s}'' = s''_{l-1} \dots s''_0$  denote by  $\mathbf{s}'\mathbf{s}''$  the concatenated string  $s'_{k-1} \dots s'_0 s''_{l-1} \dots s''_0$  of length  $k+l$ . If a string  $\mathbf{s}$  is not a head ( $\mathbf{s} \in \mathcal{S} \setminus \mathcal{W}$ ), by ignoring all  $\ominus$  symbols at the left end of  $\mathbf{s}$ , it can be converted into the corresponding (possibly empty) head,

$$\mathbf{s} \mapsto \mathbf{w} \equiv \langle \mathbf{s} \rangle \in \mathcal{W}. \tag{1.2}$$

One might think of the map  $\langle \cdot \rangle : \mathcal{S} \rightarrow \mathcal{W}$  as a projection.

Similarly, for integer  $m \geq 0$ ,  $\ell \geq 0$ , let

$$[\cdot]_\ell^m : \mathcal{W} \rightarrow \mathcal{S}_m \stackrel{\text{def}}{=} \{\oplus, \ominus\}^{m+1}$$

be the projection map returning the  $(m+1)$ -symbol substring of monomers in  $\mathbf{s}$  indexed by  $\ell, \ell+1, \dots, \ell+m$ ; equivalently, the map such that

$$\mathbf{w} = w_k \dots w_0 \mapsto [\mathbf{w}]_\ell^m \equiv \mathbf{s} = s_m \dots s_0, \quad (1.3)$$

where  $s_j = w_{\ell+j}$  for  $j \in \{0, \dots, m\}$ , and we assume that the word  $\mathbf{s}$  is extended with  $\ominus$  monomers on the left if necessary, *i.e.*, we put  $s_j = \ominus$  for all  $j$  satisfying  $k - \ell < j \leq m$ . If  $\ell = 0$ , write  $[\mathbf{w}]^m = [\mathbf{w}]_0^m$  for the word consisting of the  $m+1$  right-most monomers in  $\mathbf{w}$ , again extended with  $\ominus$  on the left if necessary. Further, if  $\mathbf{w} = w_k \dots w_1 w_0$  write  $[\mathbf{w}]^0 \equiv [\mathbf{w}]_0^0$  for its right-most monomer  $w_0$  and use  $[\mathbf{w}]_1$  to denote the shortened version  $\mathbf{w}' = w_k \dots w_1$  of  $\mathbf{w}$  without its right-most monomer  $w_0$ . If  $\mathbf{w} = \emptyset$ , we also use  $[\emptyset]_1 = \emptyset$  to indicate the fact that a microtubule without  $\oplus$  monomers loses its right-most  $\ominus$  monomer.

The state  $\mathbf{y}_t$  of the microtubule at time  $t \geq 0$  can be completely described by specifying its head  $\mathbf{w}_t = w_k(t) \dots w_0(t)$  and the position  $x_t \in \mathbb{Z}$  of its right-most symbol  $w_0(t)$ ; clearly, for every  $t \geq 0$ ,

$$\mathbf{y}_t \equiv (x_t, \mathbf{w}_t) \quad (1.4)$$

is an element of  $\mathcal{Y} \equiv \mathbb{Z} \times \mathcal{W}$ . The dynamics introduced below turns  $\mathbf{y}_t$  into a Markov process in  $\mathcal{Y}$ . Without loss of generality we may and often shall assume that the initially  $\mathbf{y}_t$  starts from the empty head located at the origin,

$$\mathbf{y}_0 = (x_0, \mathbf{w}_0) = (0, \emptyset). \quad (1.5)$$

Given positive constants  $\lambda^+, \lambda^-, \mu^+$  and  $\mu^-$ , the dynamics of  $\mathbf{y}_t$  is formally defined as follows. For arbitrary  $\mathbf{w} \in \mathcal{W}$ ,  $\mathbf{w}' \in \mathcal{W}_+$  and  $\mathbf{w}'' \in \mathcal{W}_-$ , let

$$\begin{aligned} (x, \mathbf{w}') &\mapsto (x+1, \mathbf{w}' \oplus), & \text{rate } \lambda^+, \\ (x, \mathbf{w}'') &\mapsto (x+1, \mathbf{w}'' \oplus), & \text{rate } \lambda^-, \\ (x, \mathbf{w} \oplus) &\mapsto (x-1, \mathbf{w}), & \text{rate } \mu^+, \\ (x, \mathbf{w} \ominus) &\mapsto (x-1, \mathbf{w}), & \text{rate } \mu^-, \\ (x, \mathbf{w}) &\mapsto (x, \langle \hat{\mathbf{w}} \rangle), & \text{rate } \|\mathbf{w}\|, \end{aligned}$$

where for  $\|\mathbf{w}\| > 0$  the word  $\langle \hat{\mathbf{w}} \rangle$  is obtained from  $\mathbf{w}$  by replacing one of its  $\oplus$  monomers, chosen uniformly at random, with the  $\ominus$  monomer (and then, if necessary, ignoring all its  $\ominus$  monomers on the left; recall (1.2)). Notice that as a result of the last move the number  $\|\mathbf{w}\|$  of  $\oplus$  monomers in  $\mathbf{w}$  decreases by one,  $\|\langle \hat{\mathbf{w}} \rangle\| = \|\mathbf{w}\| - 1$ , and, if the left-most  $\oplus$  monomer in  $\mathbf{w}$  transforms into  $\ominus$ , the new head is shorter,  $|\langle \hat{\mathbf{w}} \rangle| < |\mathbf{w}|$ , or might even become empty,  $\langle \hat{\mathbf{w}} \rangle = \emptyset$ . Of course, in the case  $\|\mathbf{w}\| = 0$ , the last move occurs at rate 0 (*i.e.*, almost certainly does not occur). In what follows, we write  $P(\cdot)$  and  $E(\cdot)$  for the probability distribution and the expectation related to the process  $\mathbf{y}_t$ .

If  $\mu^+ = 0$ , we recover the original version of the model studied in [1, 5, 7]. As we shall see below, the results of [5, 7] extend to the general case  $\mu^+ > 0$ , which is more realistic. In particular, the long term behaviour of the microtubule is controlled by its velocity,

$$v = \lim_{t \rightarrow \infty} \frac{x_t - x_0}{t}, \quad (1.6)$$

where the limit exists with probability one. In full analogy with the results in [5, 7], the velocity  $v$  is an analytic function of positive rates  $\lambda^+$ ,  $\lambda^-$ ,  $\mu^+$  and  $\mu^-$ ; moreover, for  $\lambda^- \geq \lambda^+$  it also possesses natural monotonicity properties as a function of these rates. Notice, however, that while (1.6) is just a law of large numbers for the coordinate process  $(x_t)_{t \geq 0}$ , the increments  $x_t - x_s$  with  $0 < s < t$  over non-overlapping intervals  $[s_i, t_i]$  are not independent. Together with the surprising result in [6] on the partial case  $\mu^+ = 0$  of the model, this suggests that the ‘natural’ monotonicity properties of the velocity  $v$  do not extend to the entirety of the parameter space  $\lambda^\pm > 0$ ,  $\mu^\pm > 0$ .

To study  $(\mathbf{y}_t)_{t \geq 0}$ , it is convenient to introduce two auxiliary processes. First, let  $0 = \tilde{\tau}_0 < \tilde{\tau}_1 < \dots$  be the times of consecutive returns of the Markov process  $\mathbf{y}_t$  to states with empty head (*i.e.*, when the microtubule loses its last  $\oplus$  monomer), and let

$$\tilde{\mathbf{y}}_\ell \equiv \mathbf{y}_{\tilde{\tau}_\ell} = (\tilde{x}_\ell, \emptyset) \equiv (x_{\tilde{\tau}_\ell}, \emptyset), \quad \ell \geq 0. \quad (1.7)$$

The jump chain  $(\tilde{\mathbf{y}}_\ell)_{\ell \geq 0}$  can clearly be identified with the process  $(\tilde{\mathbf{x}}_\ell)_{\ell \geq 0}$ , where  $\tilde{\mathbf{x}}_0 = 0$ . As we shall see in Sect. 2.1, the increments

$$(\Delta_\ell \tilde{x}, \Delta_\ell \tilde{\tau}) \equiv (\tilde{x}_\ell - \tilde{x}_{\ell-1}, \tilde{\tau}_\ell - \tilde{\tau}_{\ell-1}), \quad \ell \geq 1,$$

are independent identically distributed (*i.i.d.*) vectors having exponential moments in a neighbourhood of the origin; this implies that the convergence in (1.6) is exponentially fast.

Our second auxiliary process is a ‘finite-window’ version of the process  $(\mathbf{y}_t)_{t \geq 0}$ . For a fixed integer  $m \geq 0$ , let  $[\cdot]^m : \mathcal{W} \rightarrow \{\oplus, \ominus\}^{m+1}$  be the projection map introduced above. We define a continuous-time Markov chain  $(\hat{\mathbf{y}}_t)_{t \geq 0}$  on a ‘finite’ strip  $\mathbb{Z} \times \{\oplus, \ominus\}^{m+1}$  via

$$\hat{\mathbf{y}}_t \equiv (\hat{x}_t^m, \hat{\mathbf{w}}_t^m) \equiv \hat{\mathbf{y}}_t^m \stackrel{\text{def}}{=} (x_t, [\mathbf{w}_t]^m) \quad (1.8)$$

with jumps (and rates) inherited from the microtubule process  $(\mathbf{y}_t)_{t \geq 0}$ . Clearly, the conversion move for  $\hat{\mathbf{y}}_t$  is the same as for  $\mathbf{y}_t$ , whereas the attachment move is understood as

$$(x, \hat{\mathbf{w}}) \mapsto (x+1, [\hat{\mathbf{w}} \oplus]^m),$$

and the detachment move is (with  $\odot$  denoting  $\oplus$  or  $\ominus$ )

$$(x, \hat{\mathbf{w}} \odot) \mapsto (x-1, [\ominus \hat{\mathbf{w}}]^m);$$

in the ‘finite-state’ situation here and below,  $\emptyset \in \mathcal{S}_m$  denotes the word of length  $m+1$  made of  $\ominus$  monomers only.

As above, define the velocity  $\hat{v}_m$  of  $\hat{x}_t^m$  as the almost sure limit

$$\hat{v}_m = \lim_{t \rightarrow \infty} \frac{\hat{x}_t^m - \hat{x}_0^m}{t}. \quad (1.9)$$

Since  $\hat{x}_t^m$  is an additive functional of the finite state Markov chain  $\hat{\mathbf{w}}_t^m$ , existence of this limit follows directly from the Ergodic theorem, see, *e.g.*, [9].

## 1.2 Results

Our main results are as follows. Recall that  $P(\cdot)$  and  $E(\cdot)$  are the probability distribution and the expectation (related to the process  $\mathbf{y}_t$ ). We say that  $\xi$  is an exponential random variable with parameter  $\nu > 0$  (denoted  $\xi \sim \text{Exp}(\nu)$ ), if  $P(\xi > x) = e^{-\nu x}$  for all  $x \geq 0$ . Then, clearly,  $E\xi = \frac{1}{\nu}$ . In particular,  $\eta \sim \text{Exp}(0)$  means  $P(\eta = \infty) = 1$ .

**Theorem 1.1.** *The velocity  $v$  of the process  $x_t$  is an analytic function of the positive rates  $\lambda^\pm$  and  $\mu^\pm$ . It satisfies  $v = E\tilde{x}_1/E\tilde{\tau}_1$ , and thus  $v > 0$  if  $E\tilde{x}_1 > 0$  (the microtubule grows) and  $v < 0$  if  $E\tilde{x}_1 < 0$  (the microtubule shrinks).*

**Remark 1.1.1.** Since  $\tilde{\tau}_1$  has exponential moments,  $E\tilde{\tau}_1 < \infty$ . On the other hand,  $\tilde{\tau}_1$  stochastically dominates the initial holding time  $\eta \sim \text{Exp}(\lambda^- + \mu^-)$ , so that  $E\tilde{\tau}_1 \geq E\eta = 1/(\lambda^- + \mu^-) > 0$ .

**Remark 1.1.2.** Our approach also applies to a biologically more realistic model in the spirit of [1], where  $x_t$  is restricted to the half-line  $\mathbb{Z}^+ = \{0, 1, 2, \dots\}$ . Then  $v > 0$  corresponds to the ‘phase of unlimited growth’, while  $v < 0$  corresponds to the ‘compact phase’, where  $x_t$  is a positive recurrent process.

**Remark 1.1.3.** Thanks to existence of exponential moments of  $\tilde{x}_1$ , computer evaluation of the expectation  $E\tilde{x}_1$  can be used to numerically study the phase boundary  $\{v = 0\}$  for the Markov process  $(\mathbf{y}_t)_{t \geq 0}$ .

**Theorem 1.2.** *Let  $\lambda^- \geq \lambda^+$ . Then  $v$  is a strictly monotone function of the rates  $\lambda^\pm$  and  $\mu^\pm$ , whose partial derivatives satisfy  $\partial_{\lambda^\pm} v > 0$  and  $\partial_{\mu^\pm} v < 0$ .*

**Remark 1.2.1.** Notice that while the condition  $\lambda^- \geq \lambda^+$  can be relaxed, it cannot be omitted altogether. In fact, the ‘natural monotonicity’ properties of  $v$  can break in the complementary region  $\lambda^- < \lambda^+$ . Eg., in the particular case  $\mu^+ = 0$  of the model under consideration it is known [6] that for suitably chosen  $\lambda^+$  and  $\lambda^-$  the velocity  $v$  is not monotone in  $\mu^-$ .

The growth phase  $\{v > 0\}$  can be described in terms of the instantaneous velocities  $v_+ = \lambda^+ - \mu^+$  and  $v_- = \lambda^- - \mu^-$  as follows.

**Theorem 1.3.** *Let  $v$  and  $\hat{v}_m$  be as above. If  $v_+ = v_-$ , then  $\hat{v}_m \equiv v = v_+ = v_-$ . Otherwise,*

- a) *if  $\min(v_+, v_-) > 0$ , we have  $v > 0$  and  $\hat{v}_m > 0$  for all  $m \geq 1$ ;*
- b) *if  $\max(v_+, v_-) < 0$ , we have  $v < 0$  and  $\hat{v}_m < 0$  for all  $m \geq 1$ ;*
- c) *if  $v_+ > 0 \geq v_-$ , we have  $\hat{v}_m \nearrow v$ ; in particular,  $v > 0$  if and only if  $\hat{v}_m > 0$  for all  $m$  large enough;*
- d) *if  $v_- > 0 \geq v_+$ , we have  $\hat{v}_m \searrow v$ ; in particular,  $v < 0$  if and only if  $\hat{v}_m < 0$  for all  $m$  large enough.*



**Remark 1.3.1.** It is easy to describe the ‘growth regime’  $\{\hat{v}_m > 0\}$  of  $\hat{\mathbf{y}}_t^m$  in terms of the instantaneous velocities  $v_{\pm}$  and the stationary distribution  $\hat{\pi}^m$  of the finite state Markov chain  $\hat{\mathbf{w}}_t^m$ , see below. As the latter can be obtained by solving a finite linear system, the theorem potentially provides an alternative constructive way of describing the ‘growth regime’  $\{v > 0\}$  of the main process  $\mathbf{y}_t$ . A similar property holds in the ‘compact regime’  $\{v < 0\}$ .

It is convenient to describe the ‘compact regime’  $\{v < 0\}$  in terms of the lifetimes  $T_{\oplus}$  and  $T_{\ominus}$  of the extreme monomer, formally,

$$\begin{aligned} T_{\oplus} &= \min\{t > 0 : \mathbf{y}_t = (-1, \emptyset) \mid \mathbf{y}_0 = (0, \oplus)\}, \\ T_{\ominus} &= \min\{t > 0 : \mathbf{y}_t = (-1, \emptyset) \mid \mathbf{y}_0 = (0, \ominus)\}. \end{aligned} \quad (1.10)$$

**Theorem 1.4.** Let  $\varphi_{\oplus}(s) \stackrel{\text{def}}{=} \mathbb{E}e^{-sT_{\oplus}}$  and  $\varphi_{\ominus}(s) \stackrel{\text{def}}{=} \mathbb{E}e^{-sT_{\ominus}}$  be the Laplace transforms of the lifetimes  $T_{\oplus}$  and  $T_{\ominus}$ . Then

$$v < 0 \quad \Longleftrightarrow \quad \mathbb{E}T_{\oplus} < \infty \quad \Longleftrightarrow \quad \mathbb{E}T_{\ominus} < \infty.$$

Furthermore, this is equivalent to finiteness of  $\varphi_{\oplus}(s)$  and  $\varphi_{\ominus}(s)$  for some  $s < 0$  (i.e., both  $T_{\oplus}$  and  $T_{\ominus}$  have finite exponential moments in a neighbourhood of the origin).

**Remark 1.4.1.** For fixed positive rates  $\lambda^{\pm}$  and  $\mu^{\pm}$  it is easy to see that  $\mathbb{E}T_{\oplus}$  and  $\mathbb{E}T_{\ominus}$  are both finite or both infinite. This follows from the facts that: on the event  $\{T_{\oplus} < \infty\}$  there is a positive probability that the extreme  $\oplus$  monomer hydrolyses before any other move thus reducing the evolution of the model to the event  $\{T_{\ominus} < \infty\}$ ; similarly, on the event  $\{T_{\ominus} < \infty\}$ , with positive probability the first move results in attachment of a  $\oplus$  monomer thus reducing the evolution of the model to the event  $\{T_{\oplus} < \infty\}$ .

A similar argument shows that either both  $\varphi_{\oplus}(s)$  and  $\varphi_{\ominus}(s)$  are finite for some  $s < 0$  or they are both infinite for all  $s < 0$ , see Sect. 5.

**Remark 1.4.2.** The equivalence of  $v < 0$  and finiteness of  $\varphi_{\ominus}(s)$  for some  $s < 0$  requires a more delicate argument. Starting from the initial condition  $\mathbf{y}_0 = (0, \emptyset)$  define the times  $0 = T_0 < T_1 < T_2 < \dots$  by

$$T_k = \min\{t \geq 0 : \mathbf{y}_t = (-k, \emptyset)\}.$$

Notice that the consecutive increments  $T_k - T_{k-1}$ ,  $k \geq 1$ , are independent and have the same distribution as  $T_{\ominus}$ ; moreover, the collection  $\{T_k\}_{k \geq 0}$  is included in the collection  $\{\tilde{\tau}_{\ell}\}_{\ell \geq 0}$  from (1.7).

Now, if  $\varphi_{\ominus}(s)$  is finite in a neighbourhood of the origin, then  $\mathbb{E}T_{\ominus} < \infty$  and therefore the almost sure limit of  $\frac{1}{t}x_t$  along the infinite sequence of times  $t = T_k$  exists and must coincide with that in (1.6), implying  $v = -1/\mathbb{E}T_{\ominus}$ . On the other hand, since the trajectory  $x_t$  is exponentially concentrated around its mean  $vt$  (see Lemma 2.2 below), for  $v < 0$  this implies that the event  $\{T_1 > t\} \subseteq \{x_t \geq 0\}$  has exponentially decaying probability as  $t \rightarrow \infty$ ; hence,  $T_1 \sim T_{\ominus}$  has

finite exponential moments in a neighbourhood of the origin and the relation  $v = -1/ET_\ominus$  follows as before. For details, see Sect. 5.

We stress that it is the special property of the model, namely, existence of exponential moments for the increments (2.1), in turn implying the exponential concentration property in Lemma 2.2, which makes this argument work. This key property of the increments (2.1) guarantees that the collection of points  $(\tilde{\tau}_\ell, \tilde{x}_\ell)_{\ell \geq 0}$  is dense enough to capture the long term behaviour of the whole trajectory  $(x_t)_{t \geq 0}$ , irrespectively of the values of the rates  $\lambda^\pm$  and  $\mu^\pm$ .

The key distinction between the  $v < 0$  and  $v > 0$  cases is as follows. If  $v < 0$  the collection  $\{T_k\}_{k \geq 0}$  is a relatively dense sub-collection of  $\{\tilde{\tau}_\ell\}_{\ell \geq 0}$  and hence provides a representative sequence of times which capture the long-term behaviour of the trajectories  $\mathbf{y}_t$  during the shrinking regime. On the other hand, if  $v > 0$ , only a finite number of  $T_k$  are finite and therefore the collection of times  $\{T_k\}_{k \geq 0}$  cannot capture the long-term behaviour of the dynamics; this is, of course, compatible with the fact that in the growth regime the typical microtubule grows indefinitely and thus cannot get ‘too much shorter’ compared to its initial state.

The rest of the paper is organised as follows. In Sect. 2 we introduce and analyse the renewal decomposition of the microtubule trajectories  $\mathbf{y}_t$ , and prove Theorem 1.1. The stationary distribution of the Markov chain  $\mathbf{w}_t$  in  $\mathcal{W}$  together with that of a finite-window projection of  $\mathbf{w}_t$  are studied in Sect. 3; as a result, we deduce Theorem 1.3. In Sect. 4 we extend the previous constructions and derive the strict monotonicity property of the velocity from Theorem 1.2. Finally, Theorem 1.4 is verified in Sect. 5.

## 2 The renewal structure

The times  $0 = \tilde{\tau}_0 < \tilde{\tau}_1 < \dots$  of consecutive returns of the Markov process  $\mathbf{y}_t$  to states with empty head introduce a natural renewal structure on its trajectories. As in [5, 7], its long term properties can be deduced from the single cycle distribution.

### 2.1 Single cycle estimate

Let times  $0 = \tilde{\tau}_0 < \tilde{\tau}_1 < \dots$  be as defined above. By the strong Markov property, the increments

$$(\Delta_\ell \tilde{x}, \Delta_\ell \tilde{\tau}) \equiv (\tilde{x}_\ell - \tilde{x}_{\ell-1}, \tilde{\tau}_\ell - \tilde{\tau}_{\ell-1}), \quad \ell \geq 1, \quad (2.1)$$

are independent and identically distributed. The following result is a key to the analysis below.

**Lemma 2.1.** *The random vectors (2.1) share a common distribution with finite exponential moments in a neighbourhood of the origin.*

A simple corollary of this result is that the discrete time random walk  $(\tilde{x}_\ell)_{\ell \geq 0}$  in  $\mathbb{Z}$  generated by the *i.i.d.* steps  $\Delta_\ell \tilde{x}$  exhibits a variety of classical results, including the (strong) law of large numbers, the (local) central limit theorem and the large deviation principle. Moreover, the coordinate process  $x_t$  itself has the following concentration property.

**Lemma 2.2.** *Denote  $v = \mathbb{E}\tilde{x}_1/\mathbb{E}\tilde{\tau}_1$ . There is positive  $t_0$  (depending on the rates  $\lambda^\pm$  and  $\mu^\pm$ ) such that for every  $\varepsilon > 0$  there exist positive constants  $A = A(t_0, \varepsilon)$  and  $a = a(t_0, \varepsilon)$  so that, uniformly in  $t \geq t_0$ , we have*

$$\mathbb{P}(|x_t - vt| > \varepsilon t) \leq Ae^{-at}.$$

*Proof of Lemma 2.1.* Fix arbitrary positive rates  $\lambda^+$ ,  $\lambda^-$ ,  $\mu^+$  and  $\mu^-$ , and let  $Y_t$  be the birth-and-death process with birth rate  $\lambda = \max(\lambda^+, \lambda^-)$  and death rate 1 per individual. Following the approach of [7, Sect. 2.1] one can couple  $\mathbf{y}_t = (x_t, \mathbf{w}_t)$  and  $Y_t$  so that the number  $\|\mathbf{w}_t\|$  of  $\oplus$  monomers in  $\mathbf{w}_t \equiv \mathbf{w}(t)$ ,

$$\|\mathbf{w}_t\| \stackrel{\text{def}}{=} \sum_{j \geq 0} \mathbb{1}_{\{w_j(t) = \oplus\}}, \quad (2.2)$$

is stochastically dominated above by the total number of individuals  $Y_t$  for all  $t \geq 0$  (provided the initial conditions satisfy  $\|\mathbf{w}_0\| \leq Y_0$ ).

Let  $\mathbf{y}_t$  start from the initial state  $\mathbf{y}_0 = (0, \emptyset)$ . We are going to show that the joint generating function (cf. (1.7))

$$\Phi_0(z, s) \stackrel{\text{def}}{=} \mathbb{E}_{(0, \emptyset)}(z^{\tilde{x}_1} e^{s\tilde{\tau}_1})$$

is finite for some  $z > 1$  and  $s > 0$ . Applying the strong Markov property at the end of the initial holding time  $\eta_0 \sim \text{Exp}(\lambda^- + \mu^-)$ , we obtain

$$\Phi_0(z, s) = \frac{\mu^-}{(\lambda^- + \mu^-) - s} z^{-1} + \frac{\lambda^-}{(\lambda^- + \mu^-) - s} z \Phi_1(z, s), \quad (2.3)$$

where  $\Phi_1(z, s) = \mathbb{E}_{(0, \oplus)}(z^{\tilde{x}_1} e^{s\tilde{\tau}_1})$ ; it is thus sufficient to show that  $\Phi_1(z, s)$  is finite for some  $z > 1$  and small enough  $s > 0$ .

Consider a coupling of  $\mathbf{y}_t$  starting from  $\mathbf{y}_0 = (0, \oplus)$  and  $Y_t$  with  $Y_0 = 1$  such that  $\|\mathbf{w}_t\| \leq Y_t$  for all  $t \in [0, \tilde{\tau}_1]$ . Let  $\sigma_0$  be the time and  $\kappa_0$  be the number of jumps until  $Y_t$  hits 0, and let

$$x_1^m = \max_{t \in [0, \tilde{\tau}_1]} x_t. \quad (2.4)$$

By the coupling,  $0 < \tilde{\tau}_1 \leq \sigma_0$  and  $x_t \in [0, x_1^m] \subseteq [0, \kappa_0]$  for all  $t \in [0, \tilde{\tau}_1]$ , so that for all  $z > 0$  and  $s > 0$

$$\mathbb{E}_{(0, \oplus)}(z^{\tilde{x}_1} e^{s\tilde{\tau}_1}) \leq \mathbb{E}_{(0, \oplus)}(z^{x_1^m} e^{s\tilde{\tau}_1}) \leq \mathbb{E}_{Y_0=1}(z^{\kappa_0} e^{s\sigma_0}). \quad (2.5)$$

By the well known property of birth-and-death processes, the last expression in (2.5) is finite for suitably chosen  $z > 1$  and  $s > 0$ ; hence, the same holds for  $\Phi_1(z, s)$  and  $\Phi_0(z, s)$ . For details, see [7, Sect. 2.2].  $\square$   $\square$

**Remark 2.1.1.** Let  $\#$  be the total number of  $\oplus$  monomers attached to  $\mathbf{w}_t$  during time  $[0, \tilde{\tau}_1)$ . It is easy to see that  $2\# \leq \kappa_0 + 1$ . Further, if  $\tilde{\kappa}_1$  is the total number of jumps for the process  $\mathbf{y}_t$  starting from  $(0, \oplus)$  to first hit an empty head state  $(\tilde{x}_1, \emptyset)$ , we have  $\tilde{\kappa}_1 < 3\#$ . Consequently, for positive  $z, u, s$  the coupling above gives

$$\mathbb{E}_{(0, \oplus)}(z^{\tilde{x}_1} u^{\tilde{\kappa}_1} e^{s\tilde{\tau}_1}) \leq u^{3/2} \mathbb{E}_{(0, \oplus)}((zu^{3/2})^{\kappa_0} e^{s\sigma_0}),$$

and by choosing  $z > 1, u > 1$  so that  $zu^{3/2} > 1$  is small enough, and  $s > 0$  as in the proof of the lemma, we deduce that the expectation on the left is finite. A straightforward application of the dominated convergence theorem shows that

$$\limsup_{K \rightarrow \infty} \mathbb{E}_{(0, \emptyset)}(z^{\tilde{x}_1} e^{s\tilde{\tau}_1} \mathbb{I}_{\tilde{\kappa}_1 > K}) = 0 \quad (2.6)$$

for  $z > 1$  and  $s > 0$  as chosen above.

**Remark 2.1.2.** The construction in the proof of Lemma 2.1 has a number of useful generalisations, of which we mention the following. Let  $(\mathbf{y}'_t, \mathbf{y}''_t)$  be a dynamics in  $\mathcal{Y} \times \mathcal{Y}$  such that individual processes  $\mathbf{y}'_t = (x'_t, \mathbf{w}'_t)$  and  $\mathbf{y}''_t = (x''_t, \mathbf{w}''_t)$  in  $\mathcal{Y}$  describe a microtubule dynamics with respective collections of rates  $(\lambda_1^+, \lambda_1^-, \mu_1^+, \mu_1^-)$  and  $(\lambda_2^+, \lambda_2^-, \mu_2^+, \mu_2^-)$ . Let, further,  $Y_t$  be a birth-and-death process with birth rate  $\lambda$  and individual death rate 1. If

$$\lambda \geq \max(\lambda_1^+, \lambda_1^-) + \max(\lambda_2^+, \lambda_2^-),$$

a straightforward modification of the above construction provides a coupling  $(\mathbf{y}'_t, \mathbf{y}''_t, Y_t)$  such that the bound

$$\max(\|\mathbf{w}'_t\|, \|\mathbf{w}''_t\|) \leq Y_t$$

holds for all  $t > 0$ , provided it holds for  $t = 0$ . In fact, if  $(\mathbf{y}'_t, \mathbf{y}''_t)$  follows the maximal coupling of  $\mathbf{y}'_t$  and  $\mathbf{y}''_t$ , the above constraint can be weakened to  $\lambda \geq \max(\lambda_1^+, \lambda_2^+, \lambda_1^-, \lambda_2^-)$ .

*Proof of Lemma 2.2.* Since both  $\tilde{\tau}_\ell$  and  $\tilde{x}_\ell$  can be written as sums of *i.i.d.* increments with finite exponential moments, by the standard large deviation principle [2, 3] and Lemma 2.1, for every  $\delta > 0$  there exist positive  $B$  and  $b$  so that for all integer  $k \geq 1$ ,

$$\mathbb{P}(|\tilde{x}_k - k\mathbb{E}\tilde{x}_1| > \delta k) \leq B e^{-bk}, \quad \mathbb{P}(|\tilde{\tau}_k - k\mathbb{E}\tilde{\tau}_1| > \delta k) \leq B e^{-bk}. \quad (2.7)$$

For  $t \geq 0$ , let  $\ell = \ell_t$  be the number of times the trajectory  $(\mathbf{w}_s)_{0 \leq s \leq t}$  returns to  $\emptyset$  (i.e.,  $\tilde{\tau}_\ell \leq t < \tilde{\tau}_{\ell+1}$ ). The concentration inequality (2.7) then implies existence of positive constants  $t_*, C$  and  $c$ , such that the estimate

$$\mathbb{P}(|\ell_t - \frac{t}{\mathbb{E}\tilde{\tau}_1}| > \varepsilon t) \leq C e^{-ct} \quad (2.8)$$

holds for all  $t \geq t_*$ . Moreover, for any fixed  $\varepsilon > 0$ , relations (2.4)–(2.5) imply that

$$\mathbb{P}(|x_t - \tilde{x}_{\ell_t}| > \varepsilon t) \leq \mathbb{P}(x_1^m > \frac{\varepsilon}{2} t) \leq D e^{-dt} \quad (2.9)$$

for some positive constants  $D$  and  $d$ , uniformly in  $t \geq 2/\varepsilon$ .

To finish the proof of the lemma, decompose

$$x_t - vt = (x_t - \tilde{x}_{\ell_t}) + (\tilde{x}_{\ell_t} - \ell_t \mathbf{E}\tilde{x}_1) + (\ell_t - \frac{t}{\mathbf{E}\tilde{\tau}_1}) \mathbf{E}\tilde{x}_1$$

and notice that for every fixed  $\varepsilon \in (0, 3v)$

$$\begin{aligned} \mathbf{P}(|x_t - vt| > \varepsilon t) &\leq \mathbf{P}(|x_t - \tilde{x}_{\ell_t}| > \frac{\varepsilon}{3}t) + \mathbf{P}(|\ell_t - \frac{t}{\mathbf{E}\tilde{\tau}_1}| > \frac{\varepsilon}{3\mathbf{E}\tilde{x}_1}t) \\ &\quad + \mathbf{P}(|\tilde{x}_{\ell_t} - \ell_t \mathbf{E}\tilde{x}_1| > \frac{\varepsilon}{3}t \mid |\ell_t - \frac{t}{\mathbf{E}\tilde{\tau}_1}| \leq \frac{\varepsilon}{3\mathbf{E}\tilde{x}_1}t). \end{aligned} \quad (2.10)$$

The claim of the lemma is now immediate from (2.7), (2.8), and (2.9).  $\square$   $\square$

**Corollary 2.3.** *For arbitrary fixed  $\mathbf{w}_0 \in \mathcal{W}$ , let  $(\mathbf{y}_t)_{t \geq 0}$  be the microtubule process (1.4) started from  $\mathbf{y}_0 = (0, \mathbf{w}_0)$ . Then with  $t_0$  possibly also depending on  $\mathbf{w}_0$ , the claim of Lemma 2.2 remains true.*

*Proof.* Let  $\tilde{\tau}_0 = \min\{t > 0 : \mathbf{w}_t = \emptyset\}$  be the time when  $\mathbf{y}_t$  first visits a state with empty head,  $\mathbf{y}_{\tilde{\tau}_0} = (\tilde{x}_0, \emptyset)$ . The coupling construction in Lemma 2.1 shows that the number  $\|\mathbf{w}_t\|$  of  $\oplus$  monomers in  $\mathbf{w}_t$  can be stochastically dominated by the birth-and-death process  $(Y_t)_{t \geq 0}$  with  $Y_0 = \|\mathbf{w}_0\|$ , while a straightforward modification of the argument there shows that the hitting time of state 0 for  $Y_t$  has exponential moments in a neighbourhood of the origin. As a result, the consecutive times  $0 < \tilde{\tau}_0 < \tilde{\tau}_1 < \dots$  when  $\mathbf{w}_t$  visits state  $\emptyset$  form a delayed renewal system whose delay  $\tilde{\tau}_0$  and inter-arrival gaps  $\tilde{\Delta}_\ell = \tilde{\tau}_\ell - \tilde{\tau}_{\ell-1}$  have exponential tails. The result now follows via a suitable modification of the argument in Lemma 2.2.  $\square$   $\square$

**Remark 2.3.1.** Alternatively, one can couple two copies  $(Y'_t, Y''_t)$  of  $Y_t$  with  $(Y'_0, Y''_0) = (0, \|\mathbf{w}_0\|)$  in such a way that the difference  $Y''_t - Y'_t$  behaves as a pure death process. The distribution of the coupling time  $\tau^* = \min\{t > 0 : Y''_t = Y'_t\}$  is well understood; in particular,  $\tau^*$  has the same distribution as the maximum of  $\|\mathbf{w}_0\|$  independent  $\text{Exp}(1)$  random variables and  $\tau^* - \log \|\mathbf{w}_0\|$  has exponential moments in a neighbourhood of the origin. Hence, for each  $\delta > 0$  the probability

$$\mathbf{P}(\tau^* > \delta t) \leq \mathbf{P}(\tau^* - \log \|\mathbf{w}_0\| > \frac{\delta}{2}t)$$

is exponentially small uniformly in  $t \geq \frac{2}{\delta} \log \|\mathbf{w}_0\|$ . The argument then can be finished as in Lemma 2.2.

## 2.2 Proof of Theorem 1.1

The result of Theorem 1.1 now follows as in [5], thanks to a locally uniform version of (2.6).

### 3 Stationary distributions

By Lemma 2.1, the process  $\mathbf{w}_t$  (and, hence, its finite-window version  $\hat{\mathbf{w}}_t^m$  for any  $m \geq 0$ ) is a positive recurrent Markov chain. Write  $\boldsymbol{\pi}$  and  $\hat{\boldsymbol{\pi}}^m$  for the corresponding stationary distributions in  $\mathcal{W}$  and  $\mathcal{S}_m = \{\oplus, \ominus\}^{m+1}$ . It is convenient to express the velocity  $v$  in terms of the probabilities (recall (1.1))

$$\pi_+ \stackrel{\text{def}}{=} \boldsymbol{\pi}(\mathcal{W}_+) = \sum_{\mathbf{w} \in \mathcal{W}_+} \boldsymbol{\pi}(\mathbf{w}), \quad \pi_- \stackrel{\text{def}}{=} \boldsymbol{\pi}(\mathcal{W}_-) = \sum_{\mathbf{w} \in \mathcal{W}_-} \boldsymbol{\pi}(\mathbf{w}).$$

Similarly, put  $\hat{\pi}_+^0 = \boldsymbol{\pi}(\oplus) = 1 - \hat{\pi}_-^0$ , and, for  $m > 0$ , define

$$\hat{\pi}_+^m \stackrel{\text{def}}{=} \sum_{\mathbf{s} \in \mathcal{S}_{m-1}} \hat{\pi}^m(\mathbf{s}\oplus), \quad \hat{\pi}_-^m \stackrel{\text{def}}{=} \sum_{\mathbf{s} \in \mathcal{S}_{m-1}} \hat{\pi}^m(\mathbf{s}\ominus).$$

Then the following property holds.

**Lemma 3.1.** *Fix arbitrary positive  $\lambda^\pm$  and  $\mu^\pm$ . Then  $\hat{\pi}_+^m \nearrow \pi_+$  as  $m \rightarrow \infty$ , i.e., the sequence  $(\hat{\pi}_+^m)_{m \geq 0}$  is strictly increasing and converges to  $\pi_+$ .*

As in [7], it is convenient to prove the lemma in three steps. First, the non-strict monotonicity  $\hat{\pi}_+^m \leq \hat{\pi}_+^{m+1}$  is deduced from a suitable monotone coupling  $(\hat{\mathbf{w}}_t^m, \hat{\mathbf{w}}_t^{m+1})$  under which  $\hat{\mathbf{w}}_t^m \in \mathcal{W}_+$  only if  $\hat{\mathbf{w}}_t^{m+1} \in \mathcal{W}_+$ . Then, the strict monotonicity  $\hat{\pi}_+^m < \hat{\pi}_+^{m+1}$  is obtained from the Ergodic theorem and a uniformly positive lower bound of the density of the ‘discrepancy times’

$$\{s \geq 0 : \hat{\mathbf{w}}_s^m \in \mathcal{W}_-, \hat{\mathbf{w}}_s^{m+1} \in \mathcal{W}_+\}.$$

Finally, the convergence  $\hat{\pi}_+^m \rightarrow \pi_+$  follows from a suitable monotone coupling  $(\hat{\mathbf{w}}_t^m, \mathbf{w}_t)$  combined with an asymptotically vanishing (as  $m \rightarrow \infty$ ) upper bound of the long term density of the corresponding discrepancy times.

#### 3.1 Coupling of finite strings

Recall that the projection  $[\cdot]^m : \mathcal{W} \rightarrow \mathcal{S}_m = \{\oplus, \ominus\}^{m+1}$  maps every word  $\mathbf{w} \in \mathcal{W}$  onto a string  $\mathbf{s} \in \mathcal{S}_m$ , consisting of  $m+1$  right-most symbols in  $\mathcal{W}$  (extended on the left by  $\ominus$  symbols, if necessary). Two strings  $\mathbf{s}' = s'_m \dots s'_1 s'_0$  and  $\mathbf{s}'' = s''_m \dots s''_1 s''_0$  in  $\mathcal{S}_m$  are (partially) ordered (written  $\mathbf{s}' \prec_m \mathbf{s}''$ ) if

$$\forall k \in \{0, 1, \dots, m\}, \quad s'_k = \oplus \Rightarrow s''_k = \oplus.$$

In words,  $\mathbf{s}' \prec_m \mathbf{s}''$  if  $\mathbf{s}'$  can be obtained from  $\mathbf{s}''$  by possibly replacing some  $\oplus$  monomers in  $\mathbf{s}''$  with  $\ominus$  monomers. Similarly, given two strings  $\mathbf{s}' \in \mathcal{S}_{m'}$  and  $\mathbf{s}'' \in \mathcal{S}_{m''}$  with  $m' < m''$ , write  $\mathbf{s}' \prec \mathbf{s}''$  if  $\mathbf{s}' \prec_{m'} [\mathbf{s}'']^{m'}$  as strings in  $\mathcal{S}_{m'}$ , equivalently, if  $[\mathbf{s}']^{m''} \prec_{m''} \mathbf{s}''$ .

If  $\mathbf{s}' \prec \mathbf{s}''$ , let  $d(\mathbf{s}', \mathbf{s}'')$  be the right-most discrepancy between  $\mathbf{s}'$  and  $\mathbf{s}''$ ,

$$d(\mathbf{s}', \mathbf{s}'') = \min\{j \geq 0 : [\mathbf{s}']^j \neq [\mathbf{s}'']^j\}, \quad (3.1)$$

where  $d(\mathbf{s}', \mathbf{s}'') = 1 + \max(|\mathbf{s}'|, |\mathbf{s}''|)$  if the set of such indices  $j$  is empty. Arguing similarly to [7, Sect. 3.1] we obtain the following result.

**Lemma 3.2.** *There exists a coupling  $(\mathbf{s}'_t, \mathbf{s}''_t) \in \mathcal{S}_m \times \mathcal{S}_{m+1}$  starting from the empty initial condition  $(\mathbf{s}'_0, \mathbf{s}''_0) = (\emptyset, \emptyset)$  such that the following holds. For all  $t \geq 0$ , with the discrepancy distance  $d(\mathbf{s}'_t, \mathbf{s}''_t)$  defined as in (3.1), we have  $\mathbf{s}'_j(t) = \ominus$  for all  $j \geq d(\mathbf{s}'_t, \mathbf{s}''_t)$ . In particular,  $\mathbf{s}'_t \prec_m \mathbf{s}''_t$ , so that  $\hat{\pi}_+^m \leq \hat{\pi}_+^{m+1}$ .*

### 3.2 Strict monotonicity of $\hat{\pi}_+^m$

In the above coupling, let  $\tilde{T}_1 > 0$  be the time of the first return of  $(\mathbf{s}'_t, \mathbf{s}''_t)$  to the state  $(\emptyset, \emptyset)$ . Following the approach of [7, Sect. 3.2], one can show that

$$\mathbb{E} \left( \int_0^{\tilde{T}_1} \mathbb{I}_{\mathbf{s}'_0(u)=\ominus} \mathbb{I}_{\mathbf{s}''_0(u)=\oplus} du \right) > 0,$$

where  $\mathbb{I}_{\mathcal{E}}$  denotes the indicator function of an event  $\mathcal{E}$  (i.e.,  $\mathbb{I}_{\mathcal{E}}(\omega) = 1$  if  $\omega \in \mathcal{E}$  and  $\mathbb{I}_{\mathcal{E}}(\omega) = 0$  otherwise), and thus deduce the strict monotonicity property,

$$\hat{\pi}_+^{m+1} - \hat{\pi}_+^m \equiv \hat{\pi}_{\ominus, \oplus}^{m, m+1} = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{I}_{\mathbf{s}'_0(u)=\ominus} \mathbb{I}_{\mathbf{s}''_0(u)=\oplus} du > 0. \quad (3.2)$$

### 3.3 Convergence of $\hat{\pi}_+^m$

A version of the above construction can also be used to couple the original process  $\mathbf{w}_t$  and its finite-window projection  $\mathbf{s}'_t = [\mathbf{w}_t]^m$ . We then have

$$\pi_+ - \hat{\pi}_+^m = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{I}_{\mathbf{s}'_0(u)=\ominus} \mathbb{I}_{\mathbf{w}_0(u)=\oplus} du. \quad (3.3)$$

As above, the integral in the last display exhibits a renewal structure at the times  $0 = \tilde{\tau}_0 < \tilde{\tau}_1 < \dots$  when  $\mathbf{w}_t$  returns to state  $\emptyset$ . For the discrepancy event inside the integral to occur at time  $u \in [\tilde{\tau}_{\ell-1}, \tilde{\tau}_{\ell})$ , there must exist time  $s \in (\tilde{\tau}_{\ell-1}, u)$  such that  $\mathbf{w}_s = w_{m+1}(s) \dots w_1(s) w_0(s)$  with  $w_{m+1}(s) = w_0(s) = \oplus$  and during the time interval  $[s, u)$  all monomers to the right of  $w_{m+1}$  detach from  $\mathbf{w}_s$  with the monomer  $w_{m+1}(s)$  remaining in the  $\oplus$  state. This implies that during the cycle  $[\tilde{\tau}_{\ell-1}, \tilde{\tau}_{\ell})$  the process  $\mathbf{w}_t$  must make at least  $2(m+2)$  steps, the probability of which decays exponentially to 0 as  $m \rightarrow \infty$ . As a result (cf. [7, Sect. 3.3]), in the limit  $m \rightarrow \infty$ , the RHS of (3.3) goes to 0.

Together with the previous results, this finishes the proof of Lemma 3.1.

### 3.4 Proof of Theorem 1.3

For fixed  $m \geq 0$ , the ‘finite strip’ Markov process  $\hat{\mathbf{y}}_t = (\hat{x}_t^m, \hat{\mathbf{w}}_t^m)$  is an additive functional of the head process  $\hat{\mathbf{w}}_t^m$  in  $\mathcal{S}_m$ . By the Ergodic theorem [9], the corresponding velocity  $\hat{v}_m$  (recall (1.9)) can be written as a linear combination of the instantaneous velocities  $v_+ = \lambda^+ - \mu^+$  and  $v_- = \lambda^- - \mu^-$ , namely,

$$\hat{v}_m = v_+ \hat{\pi}_+^m + v_- (1 - \hat{\pi}_+^m) = v_- + (v_+ - v_-) \hat{\pi}_+^m.$$

Similarly (for details, see [7, Sect. 3]), the velocity of the full system  $\mathbf{y}_t$  satisfies

$$v = v_+ \pi_+ + v_- (1 - \pi_+) = v_- + (v_+ - v_-) \pi_+.$$

Theorem 1.3 now follows from monotonicity of the convergence  $\hat{\pi}_+^m \nearrow \pi_+$  as  $m \rightarrow \infty$ , recall Lemma 3.1.

## 4 Comparison of infinite strings

In this section we study monotonicity properties of the velocity  $v$ , recall (1.6). A particular care is needed due to interaction between the increments  $x_t - x_s$  of the coordinate process  $(x_t)_{t \geq 0}$  over non-overlapping intervals  $[s_i, t_i]$ . Our argument follows the (suitably re-organised and simplified) approach of [5].

Fix positive  $\lambda^\pm$  and  $\mu^\pm$ , and suppose that one is interested in dependence of the velocity  $v$  on the arrival rate  $\lambda^-$ . It is then convenient to compare two copies of the system with  $\lambda^-$  taking respective values  $\lambda' > 0$  and  $\lambda'' > 0$ , where  $\delta = \lambda'' - \lambda' > 0$ . For sufficiently small  $\delta$ , the additional (successful) arrivals of  $\oplus$  monomers in the  $\lambda''$ -system compared to  $\lambda'$ -system are rare and typically at most one such arrival takes place during a single cycle of the  $\lambda''$ -system. The following construction provides a key ingredient for our analysis of the velocity  $v$  as a function of its rates.

### 4.1 Relative coupling construction

Let  $\mathbf{y}'_t = (x'_t, \mathbf{w}'_t)$  and  $\mathbf{y}''_t = (x''_t, \mathbf{w}''_t)$  be two copies of the microtubule process starting from one of the following initial conditions

$$\mathbf{y}'_0 = (0, \mathbf{w}_0), \quad \mathbf{y}''_0 = (1, \mathbf{w}_0 \oplus) \quad (4.1)$$

(i.e.,  $\mathbf{y}''_0$  is  $\mathbf{y}'_0$  extended by a single  $\oplus$  monomer) or

$$\mathbf{y}'_0 = (0, \mathbf{w}_0), \quad \mathbf{y}''_0 = (1, \mathbf{w}_0 \ominus) \quad (4.2)$$

with some  $\mathbf{w}_0 \in \mathcal{W}$ , individually evolving as a microtubule process with common positive rates  $\lambda^\pm$  and  $\mu^\pm$ . Let

$$\tau = \min\{t \geq 0 : \mathbf{w}'_t = \mathbf{w}''_t = \emptyset\}$$

be the first time when both processes enter a state with empty head.

**Lemma 4.1.** *Given the initial conditions (4.1) or (4.2), there exists a coupling of  $\mathbf{y}'_t$  and  $\mathbf{y}''_t$  such that at the coupling time  $\tau$  the inequality  $x'_\tau \leq x''_\tau$  holds with probability one.*

**Remark 4.1.1.** Notice that for the initial conditions (4.1) or (4.2) we have  $x''_0 = x'_0 + 1 > x'_0$ . Our construction below assures that  $x''_t \geq x'_t$  for all  $t \in [0, \tau]$ , and hence for all  $t \geq 0$ .



Recall that every configuration  $(x, \mathbf{w}) \in \mathcal{Y}$  with, say,  $\mathbf{w} = w_{|\mathbf{w}|-1} \dots w_1 w_0$ , is a compact notation for the semi-infinite string  $\mathbf{s} = \dots s_2 s_1 s_0$  shifted by  $x$  units relative to the origin in  $\mathbb{Z}$ , write  $\mathbf{s} \sim (x, \mathbf{w})$ , where

$$s_k = \begin{cases} w_k, & k = 0, 1, \dots, |\mathbf{w}| - 1, \\ \ominus, & k \geq |\mathbf{w}|. \end{cases}$$

Let  $\mathbf{s}' \sim (x', \mathbf{w}')$  and  $\mathbf{s}'' \sim (x'', \mathbf{w}'')$  be two such strings with  $x' \leq x''$  and  $\mathbf{w}', \mathbf{w}'' \in \mathcal{W}$ . We first define  $k_r = d(\mathbf{w}', \mathbf{w}'') - 1$  (recall (3.1)), equivalently,

$$k_r = \max\{k \in [0, \max(|\mathbf{w}'|, |\mathbf{w}''|)] : w'_j = w''_j \text{ for all } j = 0, \dots, k\},$$

where we put  $k_r = -1$  if the set under consideration is empty. We then use

$$\mathbf{s}_r = \begin{cases} [\mathbf{w}']^{k_r} = [\mathbf{w}'']^{k_r}, & \text{if } k_r \geq 0, \\ \emptyset, & \text{otherwise,} \end{cases}$$

to denote the longest common right part of  $\mathbf{w}'$  and  $\mathbf{w}''$ . Further, let

$$k_l = \min\{k > k_r : s'_j = s''_{x''-x'+j} \text{ for all } j \geq k\};$$

as both  $\mathbf{s}'$  and  $\mathbf{s}''$  contain a finite number of  $\oplus$  monomers, such  $k_l \geq 0$  always exists (with probability one). Write

$$\hat{\mathbf{s}} = \dots s'_{k_l+2} s'_{k_l+1} s'_{k_l} \equiv \dots s''_{x''-x'+k_l+2} s''_{x''-x'+k_l+1} s''_{x''-x'+k_l}$$

for the common part of the strings  $[\mathbf{s}']_{k_r+1}^\infty$  and  $[\mathbf{s}'']_{k_r+1}^\infty$  properly shifted with respect to the origin in  $\mathbb{Z}$ , and let  $\mathbf{w}_l = \langle \hat{\mathbf{s}} \rangle$  be the corresponding head; of course,  $\mathbf{w}_l = \emptyset$  if  $\hat{\mathbf{s}}$  contains no  $\oplus$  monomers. We finally use

$$\mathbf{s}'_c = s'_{k_l-1} \dots s'_{k_r+1} \quad \text{and} \quad \mathbf{s}''_c = s''_{x''-x'+k_l-1} \dots s''_{k_r+1}$$

to denote the remaining ‘central parts’ of the strings  $\mathbf{s}'$  and  $\mathbf{s}''$ , with the tacit assumption that  $\mathbf{s}'_c = \emptyset$  if  $k_l = k_r + 1$ .

In the above notation, the canonical form (1.4) of strings  $\mathbf{s}'$  and  $\mathbf{s}''$  becomes

$$\mathbf{s}' \sim (x', \mathbf{w}') \equiv (x', \mathbf{w}_l \mathbf{s}'_c \mathbf{s}_r) \quad \text{and} \quad \mathbf{s}'' \sim (x'', \mathbf{w}'') \equiv (x'', \mathbf{w}_l \mathbf{s}''_c \mathbf{s}_r). \quad (4.3)$$

The relative shift of the two strings is  $x'' - x' = |\mathbf{s}''_c| - |\mathbf{s}'_c|$ ; when the values of  $x'$  and  $x''$  are not important we abbreviate the representation (4.3) as

$$(\mathbf{w}_l \mathbf{s}'_c \mathbf{s}_r : \mathbf{w}_l \mathbf{s}''_c \mathbf{s}_r), \quad (4.4)$$

while omitting any empty component. In the case of (4.1)–(4.2), we have  $\mathbf{s}'_c = \emptyset$  and the one-symbol string  $\mathbf{s}''_c$  (i.e.,  $|\mathbf{s}''_c| = 1$ ) is a  $\oplus$  monomer in (4.1) and a  $\ominus$  monomer in (4.2). In addition,  $\mathbf{s}_r$  is a sequence of (possibly several) consecutive  $\oplus$  monomers in (4.1), respectively,  $\ominus$  monomers in (4.2), while  $\mathbf{w}_l$  might be empty.

In general, if  $\|\mathbf{w}_l\| = \|\mathbf{s}'_c\| = \|\mathbf{s}''_c\| = 0$ , then  $\mathbf{w}_l = \mathbf{s}'_c = \emptyset$  while  $\mathbf{s}''_c$  is a finite string of  $\ominus$  monomers, *i.e.*,  $\mathbf{s}''$  is obtained from  $\mathbf{s}'$  by shifting it by  $|\mathbf{s}''_c| = x'' - x'$  monomers to the right. If the same moves are applied to both  $\mathbf{s}'$  and  $\mathbf{s}''$ , the relative shift will be preserved for all future times, including the coupling time  $\tau$ . Of course, if  $|\mathbf{s}''_c| = 0$ , then the infinite strings  $\mathbf{s}'$  and  $\mathbf{s}''$  coincide. As we shall see below, if the joint dynamics starts from a configuration with relative representation  $(\mathbf{w}_l \mathbf{s}_r : \mathbf{w}_l \mathbf{s}_c \mathbf{s}_r)$ , *i.e.*,  $\mathbf{s}''_c = \mathbf{s}_c$  while  $\mathbf{s}'_c = \emptyset$ , a coupling of the two microtubules can be constructed in such a way that the condition  $\mathbf{s}'_c(t) = \emptyset$  is preserved at all subsequent times. Consequently, for all  $t \in [0, \tau]$ ,

$$\|\mathbf{w}''_t\| - \|\mathbf{w}'_t\| \geq \|\mathbf{s}_c(t)\| \geq 0; \quad (4.5)$$

*i.e.*, the coupling time  $\tau$  coincides with the earliest  $t > 0$  when  $\mathbf{w}''_t = \emptyset$ .

Lemma 4.1 is a straightforward consequence of the following fact.

**Lemma 4.2.** *If the initial strings  $\mathbf{s}'$  and  $\mathbf{s}''$  are as in (4.3) with relative representation (4.4) of the type  $(\mathbf{w}_l \mathbf{s}_r : \mathbf{w}_l \mathbf{s}_c \mathbf{s}_r)$ , then there exists a coupling  $(\mathbf{y}'_t, \mathbf{y}''_t)$  with  $(\mathbf{y}'_0, \mathbf{y}''_0) \sim (\mathbf{s}', \mathbf{s}'')$  such that at the coupling time  $\tau$  the relative shift  $x''_\tau - x'_\tau$  equals  $|\mathbf{s}_c(\tau)| \geq 0$ .*

*Proof.* Given the initial condition  $(\mathbf{w}_l \mathbf{s}_r : \mathbf{w}_l \mathbf{s}_c \mathbf{s}_r)$  we proceed by induction in  $\|\mathbf{w}_l \mathbf{s}_c\|$ , the total number of  $\oplus$  monomers in the combined word  $\mathbf{w}_l \mathbf{s}_c$ .

Let  $\|\mathbf{w}_l \mathbf{s}_c\| = 0$ ; then  $\mathbf{w}_l = \emptyset$  and  $\mathbf{s}_c$  is a string of  $\ominus$  monomers of length  $|\mathbf{s}_c| \geq 0$ . If, additionally,  $\mathbf{s}_r = \emptyset$ , the joint system  $(\mathbf{y}'_t, \mathbf{y}''_t)$  has already reached the coupling event. Otherwise  $\mathbf{s}_r \in \mathcal{W}$  is not empty, and the infinite string  $\mathbf{s}''$  is just  $\mathbf{s}'$  shifted to the right by  $|\mathbf{s}_c|$  monomers; coupling  $\mathbf{y}'_t$  and  $\mathbf{y}''_t$  by using identical moves, we deduce the claim of the lemma with the shift  $|\mathbf{s}_c| \geq 0$ .

Fix now integer  $k > 0$  and suppose that the claim of the lemma has been verified for all initial configurations

$$(\mathbf{y}'_t, \mathbf{y}''_t) \sim (\mathbf{w}_l \mathbf{s}_r : \mathbf{w}_l \mathbf{s}_c \mathbf{s}_r) \quad (4.6)$$

with  $\|\mathbf{w}_l \mathbf{s}_c\| < k$  and arbitrary finite string  $\mathbf{s}_r$ . If at time  $t \geq 0$  the state of  $(\mathbf{y}'_t, \mathbf{y}''_t)$  is as in (4.6) with  $\|\mathbf{w}_l \mathbf{s}_c\| = k$ , we proceed as follows.

Case I. Let first  $\mathbf{s}_r = \emptyset$ , *i.e.*,

$$(\mathbf{y}'_t, \mathbf{y}''_t) \sim (\mathbf{w}_l : \mathbf{w}_l \mathbf{s}_c) . \quad (4.7)$$

If  $|\mathbf{s}_c| > 0$  (otherwise the two strings are identical and can be coupled as above) one of the words  $\mathbf{w}_l \mathbf{s}_c$  and  $\mathbf{w}_l$  must belong to  $\mathcal{W}_+$  and another to  $\mathcal{W}_-$ . Consider six independent exponentially distributed random variables

$$\begin{aligned} \zeta_1 &\sim \text{Exp}(\|\mathbf{w}_l\|), & \zeta_2 &\sim \text{Exp}(\|\mathbf{s}_c\|), & \zeta_3 &\sim \text{Exp}(\lambda^+), \\ \zeta_4 &\sim \text{Exp}(\lambda^- - \lambda^+), & \zeta_5 &\sim \text{Exp}(\mu^-), & \zeta_6 &\sim \text{Exp}(\mu^+) \end{aligned}$$

and put  $\zeta = \min(\zeta_1, \zeta_2, \zeta_3, \zeta_4, \zeta_5, \zeta_6)$ . Then the next move occurs at time  $t + \zeta$  and is as follows

- if  $\zeta = \zeta_1$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\langle \hat{\mathbf{w}}_l \rangle : \langle \hat{\mathbf{w}}_l \rangle \mathbf{s}_c)$ , where  $\hat{\mathbf{w}}_l$  is obtained from  $\mathbf{w}_l$  by hydrolysing one of its  $\oplus$  monomers, chosen uniformly at random;
- if  $\zeta = \zeta_2$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l : \mathbf{w}_l \hat{\mathbf{s}}_c)$ , where  $\hat{\mathbf{s}}_c$  is obtained from  $\mathbf{s}_c$  by hydrolysing one of its  $\oplus$  monomers, chosen uniformly at random;
- if  $\zeta = \zeta_3$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l \oplus : \mathbf{w}_l \mathbf{s}_c \oplus)$ , *i.e.*, a single  $\oplus$  monomer attaches to both strings.

The outcome of the remaining three moves depends on which of the words— $\mathbf{w}_l$  or  $\mathbf{w}_l \mathbf{s}_c$ —belongs to  $\mathcal{W}_+$ .

Case Ia. If  $\mathbf{w}_l \mathbf{s}_c \in \mathcal{W}_+$ , then:

- if  $\zeta = \zeta_4$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l \oplus : \mathbf{w}_l [\mathbf{s}_c]_1 \oplus)$ , *i.e.*, a single  $\oplus$  monomer attaches to  $\mathbf{y}'_t$ ;
- if  $\zeta = \zeta_5$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim ([\mathbf{w}_l]_1 : [\mathbf{w}_l]_1 \ominus \mathbf{s}_c)$ , *i.e.*, the microtubule  $\mathbf{y}'_t$  loses its right-most  $\ominus$  monomer;
- if  $\zeta = \zeta_6$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l : \mathbf{w}_l [\mathbf{s}_c]_1)$ , *i.e.*,  $\mathbf{y}''_t$  loses its right-most  $\oplus$  monomer.

As a result of a move with  $\zeta = \zeta_j$  for  $j = 1, 2, 4, 6$ , we get a new relative representation  $(\tilde{\mathbf{w}}_l \tilde{\mathbf{s}}_r : \tilde{\mathbf{w}}_l \tilde{\mathbf{s}}_c \tilde{\mathbf{s}}_r)$  with  $\|\tilde{\mathbf{w}}_l \tilde{\mathbf{s}}_c\| < k$ , and  $\tilde{\mathbf{s}}_r$  might be non-trivial if the right-most monomers of both  $\tilde{\mathbf{w}}_l$  and  $\tilde{\mathbf{w}}_l \tilde{\mathbf{s}}_c$  coincide; this can also happen for  $\zeta = \zeta_5$  provided  $[\mathbf{w}_l]_1 \in \mathcal{W}_+$ . In all these cases the claim of the lemma follows from the induction hypothesis.

Otherwise the system re-enters a configuration of the type (4.6) (if  $\zeta = \zeta_3$ ) or (4.7) (if  $\zeta = \zeta_5$  and  $[\mathbf{w}_l]_1 \in \mathcal{W}_-$ ). We finally notice that the relative shift  $|\tilde{\mathbf{s}}_c|$  increases by 1 if  $\zeta = \zeta_5$ , decreases by 1 if  $\zeta = \zeta_4$  or  $\zeta_6$  (in particular, it can happen that  $\tilde{\mathbf{s}}_c = \emptyset$ , so that both strings  $\mathbf{s}'$  and  $\mathbf{s}''$  become identical after the move), or does not change.

Case Ib. If  $\mathbf{w}_l \mathbf{s}_c \in \mathcal{W}_-$ , we put

- if  $\zeta = \zeta_4$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim ([\mathbf{w}_l]_1 \oplus : [\mathbf{w}_l]_1 \oplus \mathbf{s}_c \oplus)$ , and the system enters the case (4.6);
- if  $\zeta = \zeta_5$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l : \mathbf{w}_l [\mathbf{s}_c]_1)$ , and the system re-enters the case (4.7) (if  $[\mathbf{s}_c]_1 = \emptyset$ , then both  $\mathbf{s}'$  and  $\mathbf{s}''$  become identical);
- if  $\zeta = \zeta_6$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim ([\mathbf{w}_l]_1 : [\mathbf{w}_l]_1 \oplus \mathbf{s}_c)$ , *i.e.*,  $\mathbf{y}'_t$  loses its right-most  $\oplus$  monomer and the system re-enters the case (4.7) if  $[\mathbf{w}_l]_1 \in \mathcal{W}_+$ , or enters the case (4.6) if  $[\mathbf{w}_l]_1 \in \mathcal{W}_-$ .

To summarise, starting from a configuration as in (4.7) with  $\|\mathbf{w}_l \mathbf{s}_c\| = k$ , we get to (4.7), (4.6), or enter a configuration covered by the induction hypothesis.

Case II. Let  $(\mathbf{y}'_t, \mathbf{y}''_t) \sim (\mathbf{w}_l \mathbf{s}_r : \mathbf{w}_l \mathbf{s}_c \mathbf{s}_r)$  with  $\mathbf{s}_r \neq \emptyset$ . If  $\mathbf{y}'_t = (x'_t, \mathbf{w}_l \mathbf{s}_r)$ , let  $T_r$  be the lifetime of the string  $\mathbf{s}_r$ ,

$$T_r = \min\{\bar{t} > 0 : x'_{t+\bar{t}} = x'_t - |\mathbf{s}_r|\};$$

it is, of course, possible that  $T_r = \infty$  with positive probability. Notice that as long as  $\mathbf{s}_r \neq \emptyset$ , the only allowed move for the ‘internal’ parts  $\mathbf{w}_l \mathbf{s}_c$  (respectively,  $\mathbf{w}_l$ ) is hydrolysis of one of its  $\oplus$  monomers. We thus let

$$\zeta_1 \sim \text{Exp}(\|\mathbf{w}_l\|), \quad \zeta_2 \sim \text{Exp}(\|\mathbf{s}_c\|),$$

define  $\zeta = \min(\zeta_1, \zeta_2, T_r)$ , and proceed as follows.

- if  $\zeta = \zeta_1$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) = (\langle \hat{\mathbf{w}}_l \rangle \tilde{\mathbf{s}}_r : \langle \hat{\mathbf{w}}_l \rangle \mathbf{s}_c \tilde{\mathbf{s}}_r)$ , where  $\hat{\mathbf{w}}_l$  is obtained from  $\mathbf{w}_l$  by hydrolysing one of its  $\oplus$  monomers, chosen uniformly at random;
- if  $\zeta = \zeta_2$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) = (\mathbf{w}_l \tilde{\mathbf{s}}_r : \mathbf{w}_l \hat{\mathbf{s}}_c \tilde{\mathbf{s}}_r)$ , where  $\hat{\mathbf{s}}_c$  is obtained from  $\mathbf{s}_c$  by hydrolysing one of its  $\oplus$  monomers, chosen uniformly at random;
- if  $\zeta = T_r$ , then  $(\mathbf{y}'_{t+\zeta}, \mathbf{y}''_{t+\zeta}) \sim (\mathbf{w}_l : \mathbf{w}_l \mathbf{s}_c)$ , *i.e.*, the system revisits a configuration of the type (4.7), after which one proceeds as in **Case I** above.

Notice that in the first two cases the number of  $\oplus$  monomers decreases, so the new configuration is covered by the induction hypothesis.

To summarise, starting from a configuration as in (4.6) with  $\|\mathbf{w}_l \mathbf{s}_c\| = k$ , the joint dynamics either hits a state (4.6) with  $\|\tilde{\mathbf{w}}_l \tilde{\mathbf{s}}_c\| < k$  (and thus covered by the induction hypothesis), or reaches  $(\mathbf{w}_l : \mathbf{w}_l \mathbf{s}_c)$ , a reduced configuration of the type (4.7), from which a hydrolysis event (occurring with uniformly positive probability not smaller than  $k/(k + \lambda^- + \mu^- + \mu^+)$ ) leads to a configuration covered by the induction hypothesis. Since the latter happens with probability one, the proof of the lemma follows.  $\square$   $\square$

## 4.2 Relative shift argument

Fix arbitrary positive rates  $\lambda^\pm$  and  $\mu^\pm$ . Using the construction of Sect. 4.1 and the renewal structure of the trajectories of the process  $\mathbf{y}_t$ , we deduce the strict monotonicity of the velocity  $v = v(\lambda^+, \lambda^-, \mu^+, \mu^-)$  as a function of its rates in the whole region  $\lambda^- \geq \lambda^+$ . We follow the approach of [5, Sect. 3.2] and sketch the argument for  $\lambda^-$  dependence; the other cases are similar.

Since by Theorem 1.1 the velocity  $v$  is an analytic function of the rates, its strict monotonicity follows from the following fact.

**Lemma 4.3.** *There exist sufficiently small  $\delta_0 > 0$  and a positive constant  $c = c(\lambda^+, \lambda^- + \delta_0, \mu^+, \mu^-)$  such that the inequality*

$$v(\lambda^+, \lambda^- + \delta, \mu^+, \mu^-) - v(\lambda^+, \lambda^-, \mu^+, \mu^-) \geq c\delta > 0 \quad (4.8)$$

*holds uniformly in  $\delta \in (0, \delta_0)$ .*

*Proof.* It is convenient to merge the constructions of Sect. 4.1 and that in the proof of Lemma 2.1 to produce a coupling  $(\mathbf{y}'_t, \mathbf{y}''_t, Y_t^\delta)_{t \geq 0}$  of the microtubule processes  $\mathbf{y}'_t$  (with parameters  $\lambda^+, \lambda^-, \mu^+$ , and  $\mu^-$ ) and  $\mathbf{y}''_t$  (with parameters

$\lambda^+$ ,  $\lambda^- + \delta$ ,  $\mu^+$ , and  $\mu^-$ ) and a birth-and-death process  $Y_t^\delta$  (with birth rate  $\lambda^- + \delta$  and death rate one per individual) such that the bound

$$\max(\|\mathbf{w}'_t\|, \|\mathbf{w}''_t\|) \leq Y_t^\delta$$

holds for all  $t \geq 0$  provided it holds for  $t = 0$ , recall Remark 2.1.2. In what follows, we have  $\lambda^- \geq \lambda^+$  and  $\delta > 0$  is fixed sufficiently small.

If  $\mathbf{w}'_0 = \mathbf{w}''_0 = \emptyset$  and  $Y_0 = 0$ , write  $(\tau'_\ell)_{\ell \geq 0}$  and  $(\tau''_\ell)_{\ell \geq 0}$  for the times of consecutive returns by the processes  $\mathbf{y}'_t$  and  $\mathbf{y}''_t$  to states with empty head, similarly, let  $(\bar{\tau}_\ell)_{\ell \geq 0}$  be the times of consecutive returns to the state with no individuals ( $Y_{\bar{\tau}_\ell}^\delta = 0$ ) for the process  $Y_t^\delta$ ; then  $\tau'_0 = \tau''_0 = \bar{\tau}_0 = 0$ , and

$$\{\bar{\tau}_\ell\}_{\ell \geq 0} \subseteq \{\tau'_\ell\}_{\ell \geq 0}, \quad \{\bar{\tau}_\ell\}_{\ell \geq 0} \subseteq \{\tau''_\ell\}_{\ell \geq 0},$$

that is, when  $Y_t^\delta = 0$ , both  $\mathbf{y}'_t$  and  $\mathbf{y}''_t$  contain no  $\oplus$  monomers.

Let  $A_t^\delta$  be the arrival flow for  $Y_t^\delta$ ; clearly,  $A_t^\delta$  is a Poisson process of intensity  $\lambda^- + \delta < \lambda^- + \delta_0$ . It is convenient to think of  $A_t^\delta$  as a perturbation of an arrival Poisson flow  $A_t$  of intensity  $\lambda^-$ ; the latter is obtained from  $A_t^\delta$  by independently removing individual events with probability  $\delta/(\lambda^- + \delta) > 0$ . The removed arrivals (those that are present in  $A_t^\delta$  but not in  $A_t$ ) will be called the excess (or  $\delta$ -) arrivals. Notice that in the coupling  $(\mathbf{y}'_t, \mathbf{y}''_t, Y_t^\delta)$  every  $A_t$ -arrival corresponds to a simultaneous  $\oplus$  monomer attachment attempt in both microtubule processes, while each  $\delta$ -arrival corresponds to a  $\oplus$ -monomer attachment attempt in the process  $\mathbf{y}''_t$  only; the latter is successful provided the microtubule  $\mathbf{y}''_t$  ends with  $\ominus$  monomer (*i.e.*,  $\mathbf{w}''_t \in \mathcal{W}_-$ ).

Decompose the trajectory  $(\mathbf{y}'_t, \mathbf{y}''_t, Y_t^\delta)$  at times  $\bar{\tau}_\ell$ ,  $\ell \geq 1$ , and denote

$$\Delta_\ell A \equiv A_{\bar{\tau}_\ell} - A_{\bar{\tau}_{\ell-1}}, \quad \Delta_\ell A^\delta \equiv A_{\bar{\tau}_\ell}^\delta - A_{\bar{\tau}_{\ell-1}}^\delta, \quad \ell \geq 1.$$

The excursions arising as a result of this surgery are classified into three groups— $\mathcal{N}$ ,  $\mathcal{S}$ , and  $\mathcal{D}$ —in which the value of the difference  $\Delta_\ell A^\delta - \Delta_\ell A$  is, respectively, zero, one, or at least two. In words,  $\mathcal{N}$ ,  $\mathcal{S}$  and  $\mathcal{D}$  are the collections of excursions in  $Y_t^\delta$  with no  $\delta$ -arrivals, a single  $\delta$ -arrival, and at least two  $\delta$ -arrivals.

For fixed  $t > 0$ , let  $\ell_t = \max\{\ell \geq 0 : \bar{\tau}_\ell \leq t\}$  be the number of complete excursions made by an  $Y_t^\delta$  trajectory by time  $t$ . Denoting  $\delta_j x' = x'_{\bar{\tau}_j} - x'_{\bar{\tau}_{j-1}}$ , we decompose (recall that  $x'_0 = x''_0 = 0$  and  $\bar{\tau}_0 = 0$ )

$$x'_t = \sum_{j=1}^{\ell_t} \delta_j x' + (x'_t - x'_{\bar{\tau}_{\ell_t}}) = \mathbf{N}'_t + \mathbf{S}'_t + \mathbf{D}'_t + (x'_t - x'_{\bar{\tau}_{\ell_t}}), \quad (4.9)$$

where the increment contribution from each group is given by

$$\mathbf{N}'_t = \sum_{j=1}^{\ell_t} \delta_j x' \cdot \mathbb{1}_{j \in \mathcal{N}}, \quad \mathbf{S}'_t = \sum_{j=1}^{\ell_t} \delta_j x' \cdot \mathbb{1}_{j \in \mathcal{S}}, \quad \mathbf{D}'_t = \sum_{j=1}^{\ell_t} \delta_j x' \cdot \mathbb{1}_{j \in \mathcal{D}}.$$

Following the same approach for the process  $\mathbf{y}''_t$ , we get

$$x''_t = \mathbf{N}''_t + \mathbf{S}''_t + \mathbf{D}''_t + (x''_t - x''_{\bar{\tau}_{\ell_t}}). \quad (4.10)$$

To check (4.8), we show that for some positive constants  $A$ ,  $a$ , and  $c$ , the bound

$$\mathbb{P}(x_t'' < x_t' + c\delta t) \leq A e^{-at} \quad (4.11)$$

holds uniformly in  $\delta \in (0, \delta_0)$  and  $t$  large enough. It is achieved by term-wise comparison of the decompositions (4.9) and (4.10).

First,  $\mathbf{N}_t' \equiv \mathbf{N}_t''$  for all  $t \geq 0$ . Next, an argument similar to (2.4)–(2.5) implies that the distributions of the increments  $x_t' - x_{\bar{\tau}_{\ell t}}'$  and  $x_t'' - x_{\bar{\tau}_{\ell t}}''$  are stochastically dominated by that of the number of jumps in a single excursion in  $Y_t^\delta$ , and hence have exponential tails: for every  $\beta > 0$  there are positive  $B_0$  and  $b_0$  so that for all  $t$  large enough we have

$$\mathbb{P}(x_t' > x_{\bar{\tau}_{\ell t}}' + \beta t) \leq B_0 e^{-b_0 t}, \quad \mathbb{P}(x_t'' > x_{\bar{\tau}_{\ell t}}'' + \beta t) \leq B_0 e^{-b_0 t}. \quad (4.12)$$

Further, by [5, Proposition A.1], the expectation of each term contributing to  $\mathbf{D}_t'$  (similarly, to  $\mathbf{D}_t''$ ) is bounded above by  $c_2 \delta^2$  with some absolute constant  $c_2 > 0$ . By an estimate similar to (2.10) (or that in [5, Proposition A.2]), there exist positive constants  $C_2$ ,  $B_2$  and  $b_2$ , such that the estimates

$$\mathbb{P}(\mathbf{D}_t' > C_2 \delta^2 t) \leq B_2 e^{-b_2 t}, \quad \mathbb{P}(\mathbf{D}_t'' > C_2 \delta^2 t) \leq B_2 e^{-b_2 t} \quad (4.13)$$

hold for all  $\delta > 0$  small enough and all  $t$  large enough.

Each term contributing to  $\mathbf{S}_t''$  consists of possibly several excursions of  $\mathbf{y}_t''$ , exactly one of which has a single  $\delta$ -arrival attempt. If the latter is unsuccessful, the corresponding parts of trajectories of  $\mathbf{y}_t''$  and  $\mathbf{y}_t'$  coincide. Otherwise the joint dynamics  $(\mathbf{y}_t', \mathbf{y}_t'')$  between the time  $t_\delta$  of the successful  $\delta$ -arrival and the earliest time  $\tau_\ell'' > t_\delta$  follows the scenario treated by Lemma 4.1. In particular,

$$\mathbb{P}(\mathbf{S}_t'' \geq \mathbf{S}_t') = 1.$$

On the other hand, a simple one-trajectory bound based upon the construction in Sect. 4.1 implies that

$$\mathbb{E} \left[ ((x_{\bar{\tau}_j}'' - x_{\bar{\tau}_{j-1}}'') - (x_{\bar{\tau}_j}' - x_{\bar{\tau}_{j-1}}')) \mathbb{1}_{j \in \mathcal{S}} \right] \geq c_1 \delta$$

for some positive  $c_1$ . Therefore, an argument similar to that in the derivation of (4.13) implies that for some positive constants  $C_1$ ,  $B_1$ , and  $b_1$ , the estimate

$$\mathbb{P}(\mathbf{S}_t'' - \mathbf{S}_t' < C_1 \delta t) \leq B_1 e^{-b_1 t} \quad (4.14)$$

holds for all (fixed)  $\delta > 0$  small enough and all  $t$  large enough.

Finally, in view of the decompositions (4.9)–(4.10), the estimates (4.12)–(4.14) imply (4.11). It is then straightforward to deduce (4.8).  $\square$   $\square$

**Remark 4.3.1.** An alternative derivation of (4.8) can be obtained using the Ergodic theorem for Markov chains [9]; for details, see [5].

### 4.3 Proof of Theorem 1.2

By (4.8), the partial derivative  $\partial v / \partial \lambda_-$  is strictly positive in the region under consideration. The argument for the other parameters is similar.

## 5 Properties of the lifetimes

It remains to prove Theorem 1.4. Let lifetimes  $T_\oplus$  and  $T_\ominus$  be as in (1.10), and let  $\varphi_\oplus(s)$  and  $\varphi_\ominus(s)$  be their respective Laplace transforms. If  $\mathbf{y}_t$  starts from  $(0, \emptyset)$ , conditioning on the first move, we get

$$\varphi_\ominus(s) = \mathbb{E}(e^{-s\eta_0}) \left( \frac{\mu^-}{\lambda^- + \mu^-} + \frac{\lambda^-}{\lambda^- + \mu^-} \varphi_\oplus(s) \varphi_\ominus(s) \right), \quad (5.1)$$

where  $\eta_0 \sim \text{Exp}(\lambda^- + \mu^-)$  is the initial holding time; this implies

$$\mathbb{E}T_\ominus = \frac{1}{\lambda^- + \mu^-} + \frac{\lambda^-}{\lambda^- + \mu^-} (\mathbb{E}T_\oplus + \mathbb{E}T_\ominus).$$

Consequently, the expectations  $\mathbb{E}T_\oplus$  and  $\mathbb{E}T_\ominus$  are either both finite or both infinite; similarly, if one of the functions  $\varphi_\oplus(s)$  or  $\varphi_\ominus(s)$  is analytic in a neighbourhood of the origin, so is another. As in [7, Sect. 4.2], it is thus sufficient to verify the result in terms of  $\mathbb{E}T_\ominus$  and  $\varphi_\ominus(s)$ .

Let  $\mathbb{E}T_\ominus < \infty$  and let the process  $\mathbf{y}_t$  start from  $\mathbf{y}_0 = (0, \ominus)$ . Consider a sequence of stopping times  $0 = S_0 < S_1 < \dots$ , where for  $k \geq 1$

$$S_k = \min\{t > S_{k-1} : x_t = -k\}.$$

Clearly,  $\{S_k\}$  is a renewal sequence whose independent increments  $S_k - S_{k-1}$  have the same distribution as  $T_\ominus$ . Let  $(\bar{x}_k)_{k \geq 0}$  with  $\bar{x}_k = \bar{x}_{S_k}$  be a subwalk of  $(\tilde{x}_k)_{k \geq 0}$  observed at times  $S_k$ , recall (1.7). By the strong law of large numbers,

$$\frac{1}{k} \bar{x}_k \longrightarrow -\frac{1}{\mathbb{E}T_\ominus}$$

with probability one (as  $k \rightarrow \infty$ ), while Lemma 2.2 implies that  $v = -\frac{1}{\mathbb{E}T_\ominus} < 0$ .

Assume that  $v < 0$ . By Lemma 2.2 and the simple observation

$$\mathbb{P}(T_\ominus > t) \leq \mathbb{P}(x_t \geq 0) \leq \mathbb{P}(|x_t - vt| > \frac{|v|}{2}t),$$

there exist positive constants  $A$  and  $a$  so that the estimate

$$\mathbb{P}(T_\ominus > t) \leq A e^{-at}$$

holds for all  $t > 0$  large enough. It is then straightforward to deduce that  $\mathbb{E}e^{uT_\ominus} < \infty$ , for each  $u \in (0, a)$ , and therefore,  $\varphi_\ominus(s)$  is analytic in a neighbourhood of the origin. This finishes the proof of Theorem 1.4.  $\square$

We finally notice that, starting from  $\mathbf{y}_0 = (0, \oplus)$  and arguing as in the derivation of (5.1), we get, for all  $s > 0$ ,

$$\varphi_{\oplus}(s) = \mathbf{E}(e^{-s\eta_1}) \frac{\varphi_{\ominus}(s) + \mu^+ + \lambda^+ \mathbf{E}e^{-sT_{\oplus\oplus}}}{1 + \mu^+ + \lambda^+}, \quad (5.2)$$

where  $T_{\oplus\oplus} = \min\{t > 0 : \mathbf{y}_t = (-2, \emptyset) \mid \mathbf{y}_0 = (0, \oplus\oplus)\}$  is the lifetime of the word  $\oplus\oplus$  and  $\eta_1 \sim \text{Exp}(1 + \mu^+ + \lambda^+)$  is the initial holding time. Proceeding as in [7, Sect. 4.1] we deduce

$$\mathbf{E}e^{-sT_{\oplus\oplus}} = \varphi_{\oplus}(s)\varphi_{\ominus}(s) + (\varphi_{\oplus}(s) - \varphi_{\ominus}(s))\varphi_{\oplus}(s+1),$$

which together with (5.2) and (5.1) can be used to derive a functional relation in terms of  $\varphi_{\oplus}(s)$  and  $\varphi_{\oplus}(s+1)$ . For details, see [7, Sect. 4.1].

**Acknowledgement** This work was started when the second author (AME) visited the UK within the IAESTE exchange programme. He thanks Durham University for hospitality.

## References

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